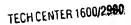


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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

PIZZA et al.

Serial No.: 09/528,682

Group Art Unit: 1654

Filing Date: March 20, 2000

Examiner: Unassigned

Title: IMMUNOGENIC DETOXIFIED MUTANT E. COLI LT-A TOXIN

TRANSMITTAL LETTER

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

Transmitted herewith for filing is an Information Disclosure Statement and a Form PTO-1449. It is believed that no fee is due.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648.

Respectfully submitted,

Date: Qua 4, 2000

By:

Dahna S. Pasternak Registration No. 41,411

Attorney for Applicants

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INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. § 1.97

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

The information listed below may be material to the examination of the above-identified application. A completed Form PTO-1449 listing the references identified below accompanies this paper.

All references are of record, or have been submitted in related application serial number 09/297,171 from which the present application claims priority under 35 U.S.C. §120. Thus, pursuant to C.F.R. §1.98(d), copies of the references are not included.

International Publication No. WO 93/13202, published July 08, 1993; International Publication No. WO 95/17211, published June 29, 1995; International Publication No. WO 96/06627, published March 07, 1996; International Publication No. WO 97/02348, published January 23, 1997; European Patent Application No. 0 145 486, published December 12, 1984;

Atty Dk o. 0342.105 USSN: 09/528,682 PATENT

Bowen et al., "Cholera Toxin Acts as a Potent Adjuvant for the Induction of Cytotoxic T-Lymphocyte Responses with Non-Replicating Antigens," *Immunology* 81:338-342 (1994):

Burnette et al., "Site-Specific Mutagenesis of the Catalytic Subunit of Cholera Toxin: Substituting Lysine for Arginine 7 Causes Loss of Activity," *Inf. & Immunity* 59(11):4266-4270 (1991);

Clements et al., "Adjuvant Activity of *Escherichia coli* Heat-Labile Enterotoxin and Effect on the Induction of Oral Tolerance in Mice to Unrelated Protein Antigens," *Vaccine* 6:269-277 (1988);

Di Tommaso et al., "Induction of Antigen-Specific Antibodies in Vaginal Secretions by Using a Nontoxic Mutant of Heat-Labile Enterotoxin as a Mucosal Adjuvant," *Inf. & Immunity* 64(3):974-979 (1996);

Domenighini et al., "MicroCorrespondence," *Mol. Microbiology* <u>15</u>(6):1165-1167 (1995);

Douce et al., "Mutants of Escherichia Coli Heat-Labile Toxin Lacking ADP-Ribosyltransferase Activity Act as Nontoxic, Mucosal Adjuvants," *Proc. Natl. Acad. Sci.* 92:1644-1648 (1995);

Douce et al., "Intranasal Immunogenicity and Adjuvanticity of Site-Directed Mutant Derivatives of Cholera Toxin," *Inf. & Immunity* 65(7):2821-2828 (1997);

Fontana et al., "Construction of Nontoxic Derivatives of Cholera Toxin and Characterization of Immunological Response Against the A Subunit," *Inf. & Immunity* 63(6):2356-2360 (1995);

Harford et al., "Inactivation of the Escherichia Coli Heat-Labile Enterotoxin by Invitro Mutagenesis," Eur. J. Biochem 183:311-316 (1989);

Holmgren et al., "An Oral B Subunit: Whole Cell Vaccine Against Cholera," *Vaccine* 10(13):911-914 (1992);

Holmgren et al., "Cholera Toxin and Cholera B Subunit as Oral-Mucosal Adjuvant and Antigen Vector Systems," *Vaccine* 11:1179-1183 (1993);

Atty Di o. 0342.105 USSN: 09/528,682 PATENT

Jackson et al., "Optimizing Oral Vaccines: Induction of Systemic and Mucosal B-Cell and Antibody Responses to Tetanus Toxoid by Use of Cholera Toxin as an Adjuvant," *Inf. & Immunity* 61(10):4272-4279 (1993);

Lycke et al., "The Adjuvant Effect of Vibrio Cholera and Escherichia Coli Heat-Labile Enterotoxins is Linked to their ADP-Ribosyltransferase," *Eur. J. Immunol*. 22:2277-2281 (1992);

Magagnoli et al., "Mutations in the A Subunit Affect Yield, Stability, and Protease Sensitivity of Nontoxic Derivatives of Heat-Labile Enterotoxin," *Inf. & Immunity* 64(12):5434-5438 (1996);

Nashar et al., "Potent Immunogenicity of the B Subunits of Escherichia Coli Heat-Labile Enterotoxin: Receptor Binding is Essential and Induces Differential Modulation of Lumphocyte Subsets," *Proc. Natl. Acad. Sci.* <u>93</u>:226-230 (1996);

Partidos et al., "The Adjuvant Effect of a Non-Toxic Mutant of Heat-Labile Enterotoxin of Escherichia Coli for the Induction of Measles Virus-Specific CTL Responses After Intranasal Co-Immunization with a Synthetic Peptide," *Immunology* 89:483-487 (1996);

Pizza et al., "Probing the Structure-Activity Relationship of Escherichia Coli LT-A by Site-Directed Mutagenesis," *Molecular Microbiology* 14(1):51-60 (1994);

Rollwagen et al., "Killed Campylobacter Elicits Immune Response and Protection When Administered With an Oral Adjuvant," *Vaccine* 11(13):1316-1320 (1993);

Snider, Denis P., "The Mucosal Adjuvant Activities of ADP-Ribosylating Bacterial Enterotoxins," *Critical Reviews in Immunology* 15(3&4):317-348 (1995);

Tsuji et al., "A Single Amino Acid Substitution in the A Subunit of Escherichia Coli Enterotoxin Results in a Loss of its Toxic Activity," *Journal of Biological Chemistry* 265(36):22520-22525 (1990);

van den Akker et al., "The Arg7Lys Mutant of Heat-Labile Enterotoxin Exhibits Great Flexibility of Active Site Loop 47-56 of the Subunit," *Biochemistry* 34:10996-11004 (1995); and

Atty Division 0342.105 USSN: 09/528,682 PATENT

Wilson et al., "Adjuvant Action of Cholera Toxin and Pertussis Toxin in the Induction of IgA Antibody Response to Orally Administered Antigen," *Vaccine* 11(2):113-118 (1993).

This Supplemental Information Disclosure Statement under 37 CFR § 1.97 is not to be construed as a representation that: (i) a complete search has been made; (ii) additional information material to the examination of this application does not exist; (iii) the information, protocols, results and the like reported by third parties are accurate or enabling; or (iv) the above information constitutes prior art to the subject invention.

Respectfully submitted,

Date: <u>Aug 4, 2000</u>

By:

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